



Europäisches Patentamt  
European Patent Office  
Office européen des brevets



Publication number: **0 521 421 A2**

(12)

## EUROPEAN PATENT APPLICATION

(21) Application number: **92110920.3**

(51) Int. Cl.<sup>5</sup>: **G01N 33/543**

(22) Date of filing: **27.06.92**

(30) Priority: **27.06.91 JP 183256/91**

(43) Date of publication of application:  
**07.01.93 Bulletin 93/01**

(84) Designated Contracting States:  
**BE CH DE FR GB IT LI NL SE**

(71) Applicant: **IDEMITSU PETROCHEMICAL  
COMPANY LIMITED**  
**1-1, Marunouchi 3-chome Chiyoda-ku  
Tokyo 100(JP)**

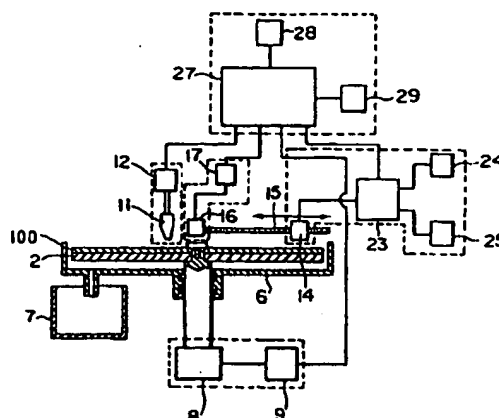
(72) Inventor: **Takase, Minoru, c/o Idemitsu  
Petrochem. Co. Ltd.**  
**1660, Kamizumi**  
**Sodegaura-shi, Chiba-ken(JP)**  
Inventor: **Shibata, Kazunori, c/o Idemitsu  
Petrochem. Co. Ltd**  
**1660, Kamizumi**  
**Sodegaura-shi, Chiba-ken(JP)**

(74) Representative: **Hoeger, Stallrecht & Partner**  
**Uhlandstrasse 14 c**  
**W-7000 Stuttgart 1(DE)**

(54) Method for analysis of liquid samples and substrate for analysis of liquid sample employed in the method.

(57) A reagent for analysis (e.g. an antibody) is fixed on a rotatable disk 100 having a plurality of channels 102. The flow paths of the channels, inclusive of reagent fixing portions 103, are treated with an aqueous solution consisting essentially of protein so that the contact angle with water is not more than 70° (104). The sample for analysis, that is a liquid sample containing an antigen, is dripped on each channel or the disk is rotated for developing the sample for analysis for reacting the reagent for analysis and the liquid sample by way of an antigen-antibody reaction, and changes produced by the reaction are measured on the disk for analysis. This results in improved fluidity of the sample for analysis in the disk-shaped sensor to improve analytic accuracy and reproducibility.

FIG. 2



EP 0 521 421 A2

## BACKGROUND OF THE INVENTION

### Field of the Invention

This invention relates to a method for analysis of liquid samples and a substrate or such analysis. More particularly, it relates to a method for analysis and a substrate for such analysis whereby analysis accuracy and reproducibility may be improved.

### Description of the Related Art

Recently, with a view to early discovery of diseases, quantitative analyses of trace amounts of components in a sample fluid are carried out frequently, in the same manner as analyses of trace amounts of samples in the field of biotechnology. In keeping with strong demands raised for analyses of liquid samples with high accuracy, various proposals have been made recently.

As a result of our eager searches in this line, the present inventors have found that, by previously coating a reagent on a rotatable disk, reacting a liquid sample with the reagent on the disk and measuring the properties of a reaction product, analyses of the liquid sample may be achieved with high accuracy and efficiency. Thus the methods for analyses of liquid samples with a disk have been arrived at and applied for patent by JP Patent Applications Nos.1-52759(1989), 1-92367 (1989) and 2-270900 (1990).

Meanwhile, with the analyses using the disk coated with the reagent (or a disk-shaped sensor), it is necessary for the samples for analyses or detection or the reagents for analyses to be allowed to flow smoothly to be developed thereon without flow-out on a plurality of sample developing surfaces formed on the surface of the disk which is formed of e.g. plastics.

However, with the above described conventional analysis for liquid samples, the surface of the disk formed of plastics, such as polycarbonate (PC) or polystyrene (PS), exhibits high hydrophobicity, so that a larger centrifugal force is required to fluidize the sample for analysis. On the other hand, because of this larger centrifugal force, it is extremely difficult to control the flow of the sample for analyses which has once started to flow, such that analytic accuracy and reproducibility cannot be increased satisfactorily.

In general, plasma discharge processing or chemical modification operations are used for surface modification of plastics. However, these processing operations are not only in need of special apparatus but are unable to maintain the effects of modification for long without considerable difficulties, although the wetting characteristics of the plastics surface can be improved transiently.

## SUMMARY OF THE INVENTION

### Object of the Invention

In view of the above depicted status of the art, it is an object of the present invention to provide a method for analysis of a liquid sample and a substrate for analyses whereby the sample for analyses put on a disk-shaped sensor may be improved in fluidity for improving analytic accuracy and reproducibility.

### Feature of the Invention

For accomplishing the above object, the present invention provides a method for analyzing a liquid sample comprising fixing a reagent for analysis on a rotatable substrate, developing a liquid sample on the substrate by dripping or rotation of the substrate for reacting the reagent for analysis with the liquid sample and measuring changes produced by the reaction on said substrate, said method further comprising treating a substrate surface inclusive of portions having said reagent for analysis fixed thereon with an aqueous solution consisting essentially of protein, preferably albumin or casein, so that the contact angle of the substrate in water is not more than 70° and preferably in the range of from 60° to 50°, and subsequently analyzing said liquid sample.

According to the present invention, the disk-shaped sensor may be improved in fluidity and non-specific reactions may be inhibited to improve analytic accuracy and reproducibility.

## BRIEF DESCRIPTION OF THE DRAWINGS

Fig.1 is a plan view showing an example of a disk-shaped sensor according to the present invention.

Fig.2 is a schematic view showing a typical apparatus for analysis employed in the method of the present invention.

Fig.3 is a schematic view showing the manner of measurement by optical analytic means.

Fig.4 is a graph showing a method for calculating the intensity of the fluorescent light in terms of the numbers of particles.

Fig.5 is a graph showing a calibration curve for CRP found in an Example.

Fig.6 is a graph showing a calibration curve for CRP found in a Comparative Example.

Figs.7(a) and 7(b) are plan views showing the states of development of samples for analysis in the Example and in the Comparative Example.

## DETAILED DESCRIPTION OF THE INVENTION